Claims

1. A library of nucleic acid molecules, each molecule comprising an open reading frame and lacking the 3'-untranslated region normally associated with said open reading frame.

2. The library of claim 1, wherein said nucleic acid is RNA.

3. The library of claim 2, wherein said RNA is messenger RNA.

4. The library of claim 2, wherein said RNA is cellular RNA.

5. The library of claim 4, wherein said cellular RNA is derived from a eukaryotic organism.

6. The library of claim 5, wherein said cellular RNA is derived from a mammal.

7. The library of claim 6, wherein said mammal is a human.

8. The library of claim 1, wherein said nucleic acid is DNA.

9. The library of claim 1, wherein said library comprises at least 10^5 members.

10. The library of claim 1, wherein said nucleic acid molecules of said

library also lack stop codons.

11. A library of nucleic acid molecules produced by the steps of:

(a) providing a library of DNA molecules, each having an open reading frame and a 3'-untranslated region, each of said DNA molecules terminating at its 5' end in an overhang and at its 3' end in a blunt end; and

(b) treating said library of DNA molecules first with a 3'→5' exonuclease and then with a single-stranded nuclease under conditions that allow removal of the 3'-untranslated regions of said DNA molecules.

12. A library of nucleic acid molecules produced by the steps of:

(a) translating a library of mRNA molecules *in vitro* in a translation reaction mixture lacking functional translation release factor activity, resulting in pausing of the translation reaction mixture ribosomes at the stop codons of said mRNA molecules;

(b) adding, to said translation reaction mixture of step (a), reverse transcriptase and oligonucleotide primers which are complementary to the 3'-untranslated regions of said mRNA molecules at a site proximal to said stop codons, under conditions which allow the synthesis of strands of DNA that are complementary to said 3'-untranslated regions and terminate at sites proximal to said stop codons; and

(c) removing the RNA portions of the RNA-DNA duplexes formed in step (b), thereby removing the 3'-untranslated regions of said mRNA molecules.

13. The library of claim 12 produced by the further steps of:

(d) ligating to each of the 3' ends of the products of step (c) a linker comprising a Type IIS restriction site;

(e) extending the products of step (d) to produce double-stranded DNA molecules; and

(f) treating said double-stranded DNA molecules with a Type IIS restriction enzyme that recognizes said Type II restriction site to cleave said DNA molecules and remove said stop codons.

14. A library of nucleic acid molecules produced by the steps of:

(a) providing a population of mRNA molecules;

(b) synthesizing strands of DNA, each of which is complementary to one of said mRNA molecules, using a random primer mixture, said random primer mixture comprising primers, each having

(i) a 3' region comprising a stop codon flanked by a random oligonucleotide located 3', 5', or both to said stop codon; and

(ii) a 5' region comprising a Type IIS restriction site;

(c) ligating to the 3' ends of the DNA products of step (b) an oligonucleotide tail;

(d) amplifying the products of step (c) using

(i) a first primer which is complementary to said Type IIS restriction site-containing sequence; and

(ii) a second primer which is complementary to said oligonucleotide tail; and

(e) treating the products of step (d) with a Type IIS restriction enzyme that recognizes said Type IIS restriction site to cleave said products, thereby removing the 3'-untranslated regions and stop codons.

15. The library of nucleic acid molecules of claim 14, produced by the further steps of:

(f) ligating a sequence which encodes an affinity tag to the cleaved ends of the products of step (e);

(g) transcribing the products of step (f);

(h) ligating peptidyl acceptors to the 3' ends of the RNA products of step (g);

(i) translating said products of step (h) to produce a population of RNA-protein fusions; and

(j) substantially isolating RNA-protein fusions which comprise said affinity tag, thereby obtaining a population of mRNA molecules lacking 3'-untranslated regions and stop codons.

16. A library of nucleic acid molecules produced by the steps of:

(a) providing a population of mRNA molecules;

(b) synthesizing strands of DNA, each of which is complementary to one of said mRNA molecules, using a random primer mixture, said random primer mixture comprising primers, each having (i) a 5' region which lacks a stop codon in at least one reading frame and (ii) a random 3' region; and

(c) synthesizing strands of DNA complementary to said DNA strands of step (b), using a second random primer mixture.

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